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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,927	10/03/2003	Steven A. Gould	02-896-A	1206

20306 7590 11/28/2006

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,927	GOULD ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25,27-31,33,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25, 27-31, 33, 34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF MENDMENT, REMARKS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment and remarks filed 09/06/06 are acknowledged, entered and considered. In view of Applicant's request claim 30 has been amended and claims 1-21, 26, 32, 35 and 39-47 have been canceled. Claims 22-25, 27-31, 33, 34 and 36-38 are now pending in the application. The objections to the specification and claims and the rejection under 35 U.S.C. 102(b) have been withdrawn in view of Applicant's amendment and remarks filed 09/06/06. However, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained for the same reasons set forth in the previous Office action.

OBJECTION TO THE CLAIM

2. Claim 22 is objected in the recitation the acronym "Hb". Use of the full terminology at least in the first occurrence would obviate this objection.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. § 103(a)

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-25, 27-31, 33, 34 and 36-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gould et al (The Journal of Trauma, Injury, Infection and Clinical Care, Vol. 43, No. 2, pp. 325-332, August 1997) taken with DeWoskin et al (U.S. Patent No. 6,498,141 and Sehgal et al (Surgery, Vol. 95, No. 4, pp. 433-438, April 1984).

Applicant's arguments filed 09/06/06 have been fully considered but they are not persuasive. Applicant has argued that the combined teachings of the prior art do not render the pending independent claims 22 and 30 *prima facie* obvious because this combination does not teach each and every element of these independent claims. The primary reference of Gould et al does not teach a method of maintaining mean circulating Hb levels about 5.0 g/dl as presently recited in independent claim 22, or a method for treating a human having a hemoglobin concentration below 7 g/dl as presently claimed in independent claim 30. Similarly, the secondary references do not

teach the methods as claimed in claims 22 and 30, and as such, they do not suggest that the sue of the hemoglobin solution for massive blood loss as presently claimed. Applicant concludes by stating that the combination does not provide a reasonable expectation of success for the presently claimed invention because the combination of these references does not teach or suggest each and every element of these claims, nor do the references provide a reasonable expectation of success of the presently claimed invention is unpersuasive.

Contrary to Applicant's arguments as discussed in the previous Office action, the primary reference Gould et a discloses like the administration of an acellular red blood cell substitute, essentially tetramer-free, crosslinked, polymerized hemoglobin solution which is free of stromal contaminants to maintain a mean circulating hemoglobin level greater than 10.0 g/dl and arterial pressure of less than 100 mm Hg due to blood loss. The prior art provides hemoglobin substitute solutions that avoid the toxicities associated with vasoconstriction, renal, hepatic and cardiac dysfunctions.

The Examiner acknowledges that the primary reference of Gould et al does not teach the administration of hemoglobin solution in an amount of at least 5L as claimed in claims 25 and 30 and the molecular weight distribution as recited in claims 24 and 38. However, with respect to the of hemoglobin solution in an amount of at least 5L as claimed in claims 25 and 30, although, the primary reference of Gould et al clearly discloses the administration of up to 6 units which is about 300 g of hemoglobin. Nevertheless, the secondary reference of DeWoskin et al ('141 patent) clearly teaches the administration/transfusion of an amount of a stroma-free, tetramer-free,

polymerized, pyridoxylated hemoglobin solution that is non-toxic to the human patient, where the amount is up to at least about 5.0 L (See e.g., abstract, col. 4, lines 20-25). The reference also states on col. 4, lines 43-63 that the infusion in amount up to at least about 5.0 L, does not cause vasoconstriction, renal toxicity, hemoglobinuria and other problems implicated with intravenous administration of known hemoglobin solutions containing physiologically undesirable amounts of tetrameric hemoglobin. The product also, is useful in the treatment of any disease or medical condition requiring a resuscitative fluid (i.e., trauma, specifically hemorrhagic shock). Thus, one of ordinary skill in the art would have been motivated at the time the invention was made to employ the product of the secondary reference of DeWoskin et al which is useful in the treatment of any disease or medical condition such as trauma or hemorrhagic shock requiring a resuscitative fluid for the intended purposes of maintaining the appropriate circulating Hb levels.

Similarly, the secondary reference of Sehgal et al teaches the transfusion of up to 900 ml (i.e. 0.9 L) of polymerization of pyridoxylated stroma free hemoglobin (poly SFH-P) to adult baboons (See e.g., abstract). Thus, in view of the secondary references teachings, and particularly in view of DeWoskin's teachings, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the administration of large volume of hemoglobin solution (i.e., up to at least about 5.0 L) into the primary reference's teachings which suggests the use of a polymerized hemoglobin solution to treat patients suffering from massive hemorrhage (i.e., bleeding) for the intended purposes of providing immediate life-sustaining therapy

until adequate red blood cell hemoglobin levels (i.e., RBC Hb concentrations) can be restored.

In regard to the molecular weight distribution of claims 24 and 38, the molecular weights are not disclosed in the primary reference; however, the claims do not define the molecular weight distribution as functional limitation, rather, the claims define the molecular weight distribution as property of hemoglobin solution. Further, the primary reference of Gould et al as well as the claimed invention has substantially the same compound/composition (i.e., acellular red blood cell substitute). Thus, the crosslinked hemoglobin solution of the primary reference would have the same molecular weight distribution as claimed because the molecular weight is an expected property, which is a characteristic when a solution is purified from the same compound/composition. Nevertheless, the prior art of the secondary reference of DeWoskin et al ('141 patent) on the Table of col. 6 discloses polymerized hemoglobin having a molecular weight distribution of a) form about 10-24% by weight of polymerized hemoglobin of polymer having molecular weight of 128 KDa, b) form about 18-30% by weight of polymerized hemoglobin of polymer having molecular weight of 192 KDa, and c) form about 45-70% by weight of polymerized hemoglobin of polymer having molecular weight of 256 KDa, which overlaps with claimed ranges of claims 24 and 38 (See also claims 1, 13, 14 and 26 of '141 patent). Similarly, the secondary reference of Sehgal et al discloses on page 435, right column, last paragraph and Figure 5, the molecular distribution of poly FSH-P in plasma ranging from 64 kDa to 600 kDa, which overlaps with the claimed ranges of 128 kDa to 256 kDa.

Therefore, in view of this and in view of the combined teachings of the prior art at the time the invention was made, one of ordinary skill in the art would have been motivated to employ a methods maintaining mean circulating Hb levels about 5.0 g/dl and a method for treating a human having a HB concentration below 7 g/dl by administering an acellular red blood cell substitute, essentially tetramer-free, crosslinked, polymerized hemoglobin solution which is free of stromal contaminants. Thus, the combined teachings of the prior art makes *prima facie* obvious methods of administering a polymerized hemoglobin solution in an amount of at least 5L having various molecular weight distributions, wherein the solution avoids the toxicities associated with vasoconstriction, and renal, pancreatic, gastrointestinal and cardiac dysfunction having total hemoglobin less than 7 g/dl, wherein said administration result in restoring adequate life-sustaining red blood cell hemosolution levels above 5.0 g/dl and arterial pressure above 60 mm Hg. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including Ex parte Harris, 748 O.G. 586; In re Rosselete, 146 USPQ 183; In re Burgess, 149 USPQ 355 and as exemplified by In re Betz, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

ACTION IS FINAL

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon Weber
Supervisory Patent Examiner

Mohamed/AAM
November 16, 2006